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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/769,699	01/25/2001	Saul J. Silverstein	6152-AJPW-AJM-EA	5342

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EXAMINER
LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
1654	14

DATE MAILED: 04/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/769,699	SILVERSTEIN ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 1/27/03 as Paper No. 13, in which claims drawn to non-elected inventions were cancelled without prejudice (claims 8, 10 and 12-23), and in which several claims were amended (claims 1, 5, 7, 9 and 11). Claims 1-7, 9 and 11 are pending in the instant application.

Any rejection of record in the previous office action, mailed 10/22/02 as Paper No. 12, that is not addressed in the instant action is withdrawn. This action is FINAL.

Sequence Compliance

Receipt is also acknowledged of a statement from applicants' representative, filed as part of Paper No. 13, that the contents of the paper sequence listing and corresponding computer readable form (CRF) submitted on 4/15/02 are the same and do not introduce any new matter into the instant specification. The application is now in sequence compliance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 9 and 11 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention. **This rejection is maintained for reasons of record in Paper No. 12, mailed 10/22/02 and repeated below.**

Each of the claims is directed towards compositions comprising a Varicella-Zoster Virus (VZV) protein, 29p. The specification teaches that the term 29p encompasses any "naturally-occurring" variant of the protein (page 9, lines 16-20). The 29p protein described in the specification comprises 1,203 amino acid residues (SEQ ID NO: 2). The specification teaches that the compositions of the invention are useful for delivery of agents into a cell for the purposes of therapy, prophylaxis, diagnosis or cell labeling. Claims 1-4, 6-7, 9 and 11 specifically recite that the 29p protein mediates delivery of an agent to a target cell. The agent can literally be of "any physical category" (e.g. page 9, lines 21-26). The target cell can be literally any cell. Thus, each claim is drawn towards a potentially broad genus of variants of SEQ ID NO: 2 that must retain the ability to bind any agent (e.g. protein, nucleic acid, liposome, carbohydrate, metal composition, etc.) and deliver the agent into literally any target cell. Thus, the claimed invention embraces an enormously broad genus of combinations of 29p variant/bound agent/target cell receptor as a critical element of the invention.

The specification and prior art do not describe what are "naturally-occurring" variants of the 29p protein described in the specification (i.e. SEQ ID NO: 2), much less which variants will retain the ability to simultaneous bind an agent and interact with a target cell such that the 29p/agent composition is delivered into the cell. For example, which domains of the protein are responsible for delivery of 29p to the cell interior? The specification describes experiments where it is shown that the protein described by SEQ ID NO: 2 can be secreted from certain cell types in vitro (e.g. human embryonic lung fibroblasts (HELF)) and that it can also enter certain

cells by endocytosis (e.g. cultured human neurons, human lymphocytes). The receptor or receptors responsible for delivery of the 29p protein into neuronal or lymphocytic cells are not described. No methods for the binding of agents (i.e. covalent or non-covalent binding) to 29p have been described by the instant specification, particularly with regard to maintaining the ability of 29p to be delivered into the cell interior via endocytosis. Therefore, the specification has not provided a structural/functional basis for one of skill in the art to envision a sufficient number of combinations of 29p variant/bound agent/target cell receptor to describe the broadly claimed genus of such combinations.

Delivery of agents into a particular target cell via linkage with 29p is a novel concept in the art and the prior art does not offset the deficiencies of the instant specification with regard to a structural/functional basis for one of skill in the art to envision combinations of 29p variant/bound agent/target cell receptor that function to deliver the agent into the target cell. Given the lack of a structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those combinations of 29p variant/bound agent/target cell receptor that meet the functional limitations of the claims, one of skill in the would not be able to envision a sufficient number of specific embodiments to describe the broadly claimed genus of such combinations. Therefore, the skilled artisan would reasonably have concluded that applicants were not in possession of the claimed invention.

Response to Arguments/Written Description

Applicant's arguments filed 1/27/03 in Paper No. 13 have been fully considered but they are not persuasive. Applicants have amended the claims to explicitly indicate that the 29p

protein is the Varicella-Zoster Virus (VZV) protein and to indicate that the target cell is a mammalian cell. The response to this rejection in Paper No. 13 essentially argues: 1) in essence the examiner asserts that neither the specification nor the prior art teach what are "naturally-occurring" variants of the 29p protein and the "agents" attached thereto, 2) it is not necessary for the specification to set forth the sequences of naturally-occurring variants of the 29p protein because the protein described by SEQ ID NO: 29 constitutes sufficient description for the genus of such proteins encompassed by the rejected claims, and because identifying additional "variants" would not require undue experimentation, 3) no structure/function relationship need be established for the claimed invention to be adequately described (e.g. the 29p protein has been shown to enter cells and methods are/were known in the art for affixing agents to a protein without eliminating the protein's functional properties), 4) the term "agent" is defined in the specification, and 5) the 29p protein does not have to have an affinity for the particular agent.

The rejection made in Paper No. 12 and repeated above is not directed solely to the issue of p29 "variants" or to the agents bound thereto in the claimed compositions and methods. While these two factors are important in considering which specific embodiments have been described, the assertion made in (1) above mischaracterizes the nature of the rejection. For example, the examiner agrees that the term "agents" has been defined in the instant specification. The rejection is made on the basis of not being able to envision a sufficient number of specific embodiments of a critical element of the claimed invention. Specifically, the rejected claims embrace a large genus of specific *combinations* of 29p variant/bound agent/target cell receptor. The rejection makes clear that applicants have not described a single embodiment where even the 29p protein described by SEQ ID NO: 2 has been modified in some fashion to bind a particular

agent (e.g. a small organic compound, protein, nucleic acid, etc.) and still retains the ability to bind to a particular cell type and mediate entry into the targeted cell. For example, at what residues on the protein described by SEQ ID NO: 2 would one covalently attach a small drug compound such that the protein retains the ability to bind to and enter a human lymphocyte? Because the instant specification and prior art does not exemplify any such manipulation of 29p (i.e. SEQ ID NO: 2) for delivery of agents, and because the instant specification does not teach which domains within the large 29p protein (1,203 amino acids) are essential for this activity, one simply cannot reliably envision those embodiments that will meet the functional limitations of the claims (i.e. binding the particular agent, binding to a particular cell and delivery of the bound agent into the cell). Therefore, even for embodiments where the protein is that described by SEQ ID NO: 2, there remains insufficient basis for one of skill in the art to envision the combination of agent and cell type that will satisfy the functional limitations of the rejected claims.

It is noted that the amendment of the claims directing the invention to mammalian cells rather than any eukaryotic cell does limit the scope of the claimed invention somewhat, but does not obviate the instant rejection. There remains no description in the prior art or instant specification as to what receptor will bind 29p and mediate its entry into the cell. Therefore, there remains no basis for one of skill in the art to envision those cell types, other than the very specific cell types described in the specification into which 29p has been shown experimentally to enter (e.g. cultured human neurons and human lymphocytes), that will allow entry of 29p into the cell. It is further noted that the amendment of the claims to read "Varicella-Zoster Virus 29p" does not alleviate the problem of 29p "variants" functional in the claimed invention

because the definition provided in the specification clearly indicates that the term 29p encompasses the VZV protein and its "variants" (page 9, lines 16-20). There remains no basis in the prior art or instant specification for one of skill in the art to envision those embodiments of the claimed invention drawn to variants of VZV that will retain the ability to enter a target cell, much less those variants that will also be able to mediate the entry of an agent bound to the variant.

The assertion that SEQ ID NO: 2 provides sufficient description of "variants" is unsupported and inaccurate. This argument appears to be an assertion that one can simply ascertain from the primary sequence of a particular protein those modifications of its structure that will allow the protein to retain activity. As indicated above, there is no basis provided by the instant specification or prior art for one to envision modifications of the protein described by SEQ ID NO: 2 (e.g. amino acid substitutions, additions or deletions) that will satisfy the functional limitations of the claims. For example, there is no description in the prior art or instant specification concerning those portions of the very large 29p protein that are essential to its ability to be taken up by particular cells. Moreover, the prior art teaches that the relationship between the sequence of a protein and its tertiary structure (in essence the structure which defines its activity), is not well understood and is not predictable, as evidenced by Berendsen (Science. 1998, Vol. 282, pages 642-643; see the entire document). This reference teaches that "Thus, one of the "grand challenges" of high-performance computer-predicting the structure of proteins-acquires much of the flavor of the Holy Grail quest of the legendary knights of King Arthur: It is extremely desirable to possess but extremely elusive to obtain." (Page 643, columns 1-2). The whole reference teaches about the unpredictability in the art concerning protein

structure, and failures to make it predictable. Thus, given the lack of description in the instant specification or prior art concerning the functional domains of the 29p protein for mediating its entry into target cells, and given the unpredictability of the art concerning envisioning the structural/functional properties of a protein from primary sequence alone, the protein described by SEQ ID NO: 2 cannot provide sufficient description of the 29p "variants" encompassed by the rejected claims.

The mere observation that 29p will enter certain cells does not provide a basis for one of skill in the art to envision those *combinations* of 29p variant/agent/target cell type that will satisfy the functional limitations of the claim, especially in the absence of a description in the prior art or instant specification concerning the functional domains of 29p and of its cell surface receptor. Assertions regarding methods known in the art for affixing agents to proteins are better suited to an enablement rejection. This rejection is made on the basis of a lack of sufficient description of specific combinations of 29p variant/agent/target cell receptor that satisfy the functional limitations of the claim. In the absence of a description of the domains or amino acid residues within SEQ ID NO: 2 that are essential for mediating 29p entry into certain cells, there remains no basis for one to reliably envision specific combinations of 29p variant/agent/target cell receptor that will satisfy the functional limitations of the claims, even if one knows theoretically how the agent might be attached to the 29p protein. Thus, the description of a structural/functional relationship of the 29p protein is critical to the ability of one of skill in the art to envision specific combinations of 29p protein/agent/target cell type that will satisfy the functional limitations of the claim.

While the examiner does state in making the rejection that "...each claim is drawn towards a potentially broad genus of variants of SEQ ID NO: 2 that must retain the ability to bind any agent..." this is not an assertion that the 29p variant must necessarily have affinity to the particular agent in the sense of a ligand for its cognate receptor, for example. The examiner is using the term "bind" in the broad sense used in the instant specification, including embodiments where the agent is covalently attached, 29p is bound by a 29p-specific protein (e.g. an antibody), the agent is enclosed within a liposome comprising 29p, etc. Even in these embodiments, there remains the issue of how the "binding" of the agent affects the 29p protein. Covalent attachment is an obvious example where attachment of the desired agent might by expected to have deleterious effects on the structural/functional characteristics of the 29p protein (see above). In another example, where the 29p protein is somehow modified to incorporate the protein into a liposome that can envelope the agent for delivery, modification of the 29p protein by incorporation of a lipid-soluble moiety into 29p so that the altered 29p is functionally displayed on the outer surface of the liposome would be unpredictable in the absence of any teachings regarding the structural/functional characteristics of 29p. Again, there remains no structural/functional basis provided by the prior art or instant specification to reliably envision sufficient specific combinations of 29p protein or variant/agent/target cell receptor that meet the functional limitations of the claimed invention to describe the broad genus of such combinations of 29p protein or variant/agent/target cell receptor encompassed by the rejected claims.

Claims 1-7, 9 and 11 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This rejection is maintained for reasons of record in Paper No. 12, mailed 10/22/02 and repeated below.**

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The invention is complex, involving the delivery of a desired compound into a desired target cell via the ability of a targeting protein to bind a receptor or receptors on the surface of the cell such that the compound is delivered into the interior of the cell. The desired agent is "bound" to the targeting protein by either covalent or non-covalent linkages (e.g. antibody binding) such that it is delivered along with the targeting protein.

Breadth of the claims: The breadth of the claims greatly exacerbates the complexity of the invention in that the claims are directed towards any target cell type and delivery of literally any agent not limited by any physical category. Thus, the claimed invention encompasses a huge combination of different compositions depending on different combinations of target cell type (i.e. receptor) and methods of binding the desired agent to the targeting protein, 29p. The claims are also broad in the sense that the specification teaches that the term "29p" includes any "naturally-occurring" variant of 29p.

Guidance of the specification/Working examples: The specification teaches that the VZF protein described by SEQ ID NO: 2 is secreted by human embryonic lung fibroblasts in vitro and

can be taken in by endocytosis by neuronal or lymphocyte cells in vitro. SEQ ID NO: 2 describes a Varicella-Zoster Virus (VZV) protein that is 1,203 amino acids in length. The specification asserts that there are numerous teachings in the prior art of how to link different compounds (e.g. nucleic acids, proteins, etc.) to a protein. No such methods are actually taught in the specification. Those portions of the protein described by SEQ ID NO: 2 that are required for endocytosis are not taught by the specification. No "naturally-occurring" variants of SEQ ID NO: 2 are taught in the specification. The receptor or receptors involved in mediating 29p-based endocytosis are not taught in the specification. There are no working examples where a desired agent of any type is bound to 29p and delivered to a target cell of any type.

State of the art: Methods of detecting entry of a protein compound into a cell are known in the art. Methods of binding different compounds to a protein are known in the art. The concept of using 29p to deliver any agent into a target cell is novel in the prior art. Thus, the prior art does not provide teachings regarding those domains of 29p that can be modified by "binding" to any agent such that 29p and the agent will be delivered into a target cell. The prior art also does not identify which receptors on which cells might be capable of binding 29p and mediating endocytosis of 29p and any bound agent. Therefore, the prior art does not offset the deficiencies of the instant specification with regard to which combinations of 29p variant/agent/target receptor or receptors will work to deliver the agent to a desired cell.

Predictability of the art: Given the lack of teachings in the prior art as to what portions of SEQ ID NO: 2 can be modified by an agent such that it can be delivered, along with a desired agent, into a particular cell, and given the lack of teachings in the prior art as to what cell receptor or receptors are involved in 29p-mediated endocytosis, it would be unpredictable a

priori as to which combinations of 29p variant/agent/cell receptor or receptors will function to mediate delivery of the agent to the targeted cell.

The amount of experimentation necessary: Given a full consideration of the factors listed above, particularly with regard to those factors that contribute to the unpredictability of the invention, it would take undue, unpredictable experimentation to make an use even one embodiment of the broadly claimed invention.

Response to Arguments/Lack of Enablement

Applicant's arguments filed 1/27/03 in Paper No. 13 have been fully considered but they are not persuasive. Applicants' response essentially argues: 1) the traversal is based in part on the arguments presented against the Written Description rejection (see above), 2) applicants disagree with the examiner's characterization of the invention as "complex", 3) applicants have narrowed the scope of the invention to delivery of an agent to only mammalian cells rather than any cell of any type, 4) the experiments taught in the instant specification where 29p is shown to enter certain cell types, in combination with known methods for affixing agents to proteins and identifying naturally occurring protein variants, would be sufficient to enable the skilled artisan to practice the claimed invention without undue experimentation, and 5) while the use of 29p as a means to deliver an agent to a target cell is novel in the art, the art teaches that other proteins can be used to deliver agents to a desired target cell (e.g. the tat protein as taught in U.S. Patent No. 5,674,980; henceforth the '980 patent).

To the extent that applicants' response to the instant rejection for lack of enablement is based upon the arguments made by applicants in response to the written description rejection made herein against the same claims, the discussion above is incorporated here as a response to

applicants' arguments. The assertion that the invention is not complex is inaccurate. The invention involves the binding of a desired agent of literally any type to the 29p protein, or a naturally-occurring variant thereof, in such a manner that the 29p/agent complex can bind and enter a particular target cell. This involves the attachment of the agent to the 29p protein or variant thereof in such a fashion that the 29p/agent complex can still bind to the 29p receptor or receptors and mediate entry into the desired target cell. At a minimum, the invention thus encompasses a functional interaction between the 29p protein or variant with a desired agent, the functional interaction of the modified 29p protein or variant comprised within the complex with a cognate receptor on the target cell surface, and retention of the ability of the receptor bound to the 29p protein/agent complex to mediate endocytosis such that the bound agent is delivered into the cell. Thus, the invention is complex, involving the multi-functional interaction of at least three different moieties. Given the lack of any teaching in the instant specification concerning modification of the 29p protein and/or the nature of its cognate receptor(s) on the cell surface, practicing the claimed invention becomes even more complicated and unpredictable.

While the amended claims have a somewhat narrower scope, the claims remain broad in scope in that any mammalian cell can be a target cell for practicing the claimed invention and because there is only a limited subset of mammalian cells that have been shown to allow entry of 29p into the cell, with no characterization of the receptor(s) involved in the process. For example, there is no basis for assuming that neuronal cells derived from non-human sources will comprise the receptor(s) needed to mediate 29p entry into the cell. Even for human cells other than human neuronal cells or lymphocytes, there is no basis for one to extrapolate the findings to those cell types (e.g. epithelial cells or hepatocytes). Thus, limiting the scope to just mammalian

cells rather than any cell of any type, while helpful, does not obviate the instant rejection for lack of enablement.

The assertion that the experiments described in the specification where 29p is shown to enter certain types of mammalian cells (e.g. lymphocytes or neuronal cells), in combination with teachings in the art for affixing proteins to agents and for identifying protein "variants", enable one of skill in the art to practice the claimed invention without undue experimentation is inaccurate, and appears to be an argument that only routine experimentation would be required to practice the claimed invention. This argument ignores the Wands analysis presented above concerning why the experimentation required to make and use the claimed invention would be undue.

While the examiner acknowledges that certain methods were known in the art for affixing agents to a particular polypeptide and for assaying the entry of a protein into a cell, it would take undue, unpredictable experimentation to practice the claimed invention given the lack of teachings concerning the structural/functional characteristics of 29p regarding its entry into particular cells and which cell surface receptor(s) mediate 29p entry. For example, one of skill in the art would have to envision a modification of the 29p protein, or one of its "variants", that would allow the protein to "bind" the desired agent and retain still retain its ability to bind a particular cell type. One would then have to either purify 29p protein expressed during normal VZV infection and/or recombinantly express a nucleic acid encoding 29p and purify the desired protein, perform the steps needed to alter the 29p protein so that it "binds" the desired agent, and then test whether the 29p/agent complex can bind the desired cell type such that it is transported into the cell. If unsuccessful, which is likely considering the lack of teachings in the instant

specification or prior art concerning what modifications to 29p will be tolerated and what the actual cell receptor(s) are for 29p, one would have to envision a modification of the first approach (e.g. different modification of 29p or one of its variants to bind the desired agent, and/or different agent, and/or target cell), or envision an entirely new combination of 29p protein or variant/agent/target cell, and repeat the entire unpredictable experimental process of obtaining the 29p protein, modification to bind the agent and testing to assay for delivery into the target cell. Given the nature and number of steps that must be done, and the unpredictable nature of the experimentation involved in practicing the claimed invention, the experimentation required for the skilled artisan to practice the claimed invention is necessarily undue experimentation.

At no point did the examiner assert in making the rejection that the concept of using a protein to deliver a particular agent to a cell was not known in the art. The assertion that the state of the art acknowledges the concept of using a particular protein to deliver an agent into a particular cell is not challenged here (e.g. the tat fusion proteins taught in the '980 patent). Applicants' response, however, does not indicate how the teachings of the '980 patent make practicing applicants' invention any easier or more predictable. For example, there is no indication in applicants' response, the instant specification or the prior art that the HIV tat protein bears any common structural/functional features to the proteins claimed in the instant invention with regard to entering a cell. Therefore, the teachings of the '980 patent do not alleviate the experimentation required to practice the claimed invention or make such experimentation more predictable.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 9 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7, 9 and 11 are vague and indefinite in that the metes and bounds of the term "29p" are unclear. The specification states the term "29p" encompasses "...protein having the sequence identified in Figure 6 or a naturally-occurring variant thereof" (page 9, lines 16-20). The specification and prior art do not clearly indicate what is a "naturally-occurring variant" of 29p. For example, which variants of 29p that are functional are also "naturally-occurring"? Therefore, the metes and bounds of the term are unclear. It would be remedial to explicitly recite that the protein is that described in Figure 6 (i.e. SEQ ID NO: 2). **This rejection is maintained for reasons of record in Paper No. 12, mailed 10/22/02 and repeated below.**

Response to Arguments/112 2nd Paragraph

Applicant's arguments filed 1/27/03 in Paper No. 13 have been fully considered but they are not persuasive. The rejected claims have been amended to read "Varicella-Zoster Virus 29p protein". Applicants' response essentially argues that the amended claims no longer comprise the limitation of "29p" in the context objected to by the examiner. This assertion is inaccurate because the definition for the term 29p provided by the instant specification clearly indicates that the term "29p" is synonymous with "VZV ORF29p protein" (page 9, lines 16-20 of the instant specification). Thus, the rejected claims still read on "naturally-occurring variants" of the protein described in Figure 6 (SEQ ID NO: 2). The rejection stands as there is no basis for the

skilled artisan to determine whether a particular protein is a "naturally-occurring variant" of SEQ ID NO: 2.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

Ggl
April 7, 2003